REMARKS

Claims 1-9, 12-19, 23-26, 28-31 and 33-34 are pending in the subject application. Applicants have hereinabove amended claims 12-19, 23-26, 28-31 and 33 and added new claims 39-49. Support for these amendments may be found inter alia in the specification as follows: claims 39-49: originally filed claims 10-11, 20-22, 27, 32, and 35-38. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 1-9, 12-19, 23-26, 28-31 and 33-34 and 39-49 will be pending.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 1-9, 12-19, 23-26, 28-31, 33, 34 under 35 U.S.C. §103(a) as being unpatentable over the combination of Columbo in view of Mohammadi. The Examiner stated that what has been searched and considered here is: A method of preventing or treating cutaneous inflammation by inhibiting a KIT protein. The Examiner stated that Columbo (J of Immunology) entitled "The Human Recombinant c-kit Receptor Ligand, rhSCF, Induces Mediator Release From Human Cutaneous Mast Cells and Enhances IgE Dependent Medicator Release From Both Skin Mast Cells and Peripheral Blood Basophils" teaches in the abstract, a ligand for the c-kit proto oncogene receptor, a member of the tyrosine kinase receptor class, and the effects of c-kit receptor ligand stem cell factor on the release of inflammatory mediators from human skin mast cells. The Examiner stated that there were effects on mast cells related to human allergic reactions and SCF may modulate mast cells function under physiologic conditions. The Examiner stated that on page 604 column 1, antibodies which recognize human c-kit receptor is shown.

The Examiner stated that on page 606 column 2 last paragraph bridging to 607, the antibodies against c-kit receptor and their effects were discussed. The Examiner stated that the claims differ from Colombo in that they are directed to preventing or treating specifically where Columbo is measuring effects. The Examiner stated that Mohammadi (Science) entitled "Structures of the Tyrosine Kinase Domain of Fibroblast Growth Factor Receptor in Complex with Inhibitors" teaches on page 955, protein tyrosine kinases are critical components of signaling pathways and selecting inhibitors have considerable therapeutic value. The Examiner stated that it would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically treat with inhibitors as taught by Mohammadi in the method of Columbo because the inflammatory effects related to c-kit and that such effects are modifiable are taught by Columbo. The Examiner stated that Mohammadi is directed to inhibiting the same pathways as Columbo for therapeutic reasons. The Examiner stated that the connection between c-kit and cutaneous inflammation is clearly by Columbo. The Examiner stated that to select a known antibody such as ACK2 in view of Columbo who selects other antibodies would have been obvious because it would have the expected result.

In response, applicants respectfully traverse the Examiner above rejection. Applicants contend that Columbo in view of Mohammadi does not render obvious the claimed invention for the reasons which follow.

With respect to Columbo, the Examiner stated that the claims differ from the cited reference in that Columbo is measuring effects, while the claims are directed to preventing or treating. In a

similar vane, applicants would like to highlight the point that Columbo describes **in vitro** experiments, while applicants' claimed invention relates to **in vivo** methods. Columbo describes experiments which show that in vitro incubation of mast cells with SCF augments IgE-dependent mediator release from these cells. However, applicants point out that one often cannot predict what will happen in vivo based on in vitro experiments. In support, applicants respectfully direct the Examiner's attention to Ando et al. (1993) Journal of Clinical Investigation, volume 92(4):1639-1649. Applicants note that a copy of this reference was attached to the information disclosure statement filed on April 19, 2000 in connection with the subject application. Ando et al. describes in vivo experiments wherein c-kit ligand (i.e. SCF) was administered to mice. As detailed on page 1647, column 1, the in vivo results were unexpected based on Columbo's in vitro results. Ando et al further states that "the living organism is so complex in comparison to in vitro systems that it is not uncommon for in vivo experiments to produce findings that on first glance appear inconsistent with the results of work in vitro." Accordingly, applicants contend that in this system, one skilled in the art would not be able to predict what would happen in vivo based on the in vitro data. If fact, this notion is explained in the subject application on page 41, lines 5-32.

Mohammadi does not supply what is missing from the primary reference (i.e. a showing that in vitro data can be used to predict in vivo results). The Examiner cites Mohammadi to show that protein tyrosine kinases are critical components of signal transduction pathways and thus, inhibitors of such pathways could have therapeutic value. However, Mohammadi does not relate to a

mast cell system or to cutaneous inflammation. In addition, Mohammadi describes in vitro experiments. Accordingly, the teachings of Mohammadi do not overcome the fact that Columbo's in vitro results were inconsistent with Ando's in vivo results and therefore, cannot form the basis for any reasonable expectation of success in vivo. Applicants contend that based on the state of the literature prior to applicants' invention, one skilled in the art would not have been able to predict with a reasonable expectation of success that a compound which inhibits the stem cell signaling pathway would be able to prevent or treat cutaneous inflammation in subject. Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-9, 12-19, 23-26, 28-31, 33, 34 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that the elected invention is directed to preventing or treating cutaneous inflammation. The Examiner stated that applicant is invited to specifically point out where in the specification a method of preventing or treating cutaneous inflammation is found. The Examiner stated that since an election of species was made, no other issues under 35 U.S.C. §112 will be considered here regarding the presently pending claims.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that the subject application is

enabled. With respect to the Examiner's request that applicants point out where a method of preventing or treating cutaneous inflammation is found, applicants respectfully direct the Examiner's attention to page 11, line 36 to page 12, line 6 which provides that administration of a compound capable of inhibiting the stem cell factor signaling pathway can prevent or treat cutaneous inflammation. In addition, page 15, lines 14-18 provides various routes of administration of the compound. In support, applicants respectfully direct the Examiner's attention to page 41, line 34 to page 42, line 33, and in particular the paragraph beginning on page 42, line 24 which states that the findings show that blocking the SCF-KIT signaling pathway can inhibit inflammation. The experiments showed that subjects treated with the compound showed less respiratory distress compared to untreated subjects. That the administration of the compound used in the experiments, i.e. ACK2, resulted in KIT inhibition is evident by the fact that ACK2 antibody is an anti-C-KIT-antibody. Accordingly, any effect exerted by the administration of this compound is one which affects KIT. Accordingly, the application clearly shows that one can treat or prevent cutaneous inflammation by administering compounds capable of inhibiting the stem cell factor signaling pathway. Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Title

The Examiner stated that the title of the invention is not aptly descriptive. The Examiner stated that a new title is required that is clearly indicative of the invention to which the claims are directed.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein changed the title.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 1-9, 12-19, 23-26, 28-31 and 33-34 and 39-49,

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone either of them at the number provided below.

No fee other than the enclosed $2,263.00, which includes the $445.00 fee for a three-month extension of time and the $1,818.00 fee for additional claims, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

8-14-01

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